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March 18, 2002

Commissioner for Patents
Washington, D.C. 20231

Re: U.S. Patent Application Serial No. 09/780,035
Applicants: Tariq Ghayur, *et al.*
Filed: February 9, 2001
Title: *ANTIBODIES THAT BIND HUMAN INTERLEUKIN-18 AND METHODS AND USING*
Attorney Docket No.: BBI-149

Dear Sir:

I enclose herewith for filing in the above-identified application the following:

1. Response to Restriction Requirement;
2. Request for Two-Month Extension of Time;
3. Check for $400.00; and
4. A pre-paid, acknowledgment postcard.

Please charge any necessary fees to our Deposit Account No. 12-0080. The undersigned requests any extensions of time necessary to respond. A duplicate of this sheet is enclosed.

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March 18, 2002
Date

Giulio A. DeConti, Jr., Esq., Reg. No. 31,503

Respectfully submitted,

LAHIVE & COCKFIELD, LLP

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Reg. No. 31,503
Attorney for Applicants

Election/EXT(2)/#9
4.17.02

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the application of: Tariq Ghayur, *et al.*

Serial No.: 09/780,035

Filed: February 9, 2001

For: *ANTIBODIES THAT BIND HUMAN INTERLEUKIN-18 AND METHODS OF MAKING AND USING*

Attorney Docket No.: BBI-149

Group Art Unit: 1644

Examiner: Jamroz Margaret E

Commissioner for Patents
Washington, D.C. 20231

Certificate of First Class Mailing (37 CFR 1.8(a))

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3-18-2002
Date of Signature and of Mail Deposit

By: Guilio A. DeConti, Esq.
Reg. No. 31,503
Attorney for Applicants

RESPONSE TO RESTRICTION REQUIREMENT

Dear Sir:

This is in response to the restriction requirement set forth in the Office Action dated December 18, 2001 (Paper No. not specified). A separate petition for the appropriate extension of time in which to respond is being filed concurrently herewith.

The Examiner has required restriction to one of the following inventions under 35 U.S.C. §121:

I. Claims 1-2, drawn to a small molecule capable of binding a human IL-18; Class 530, subclass 500.

II. Claims 1-2 drawn to a peptide capable of binding a human IL-18; classified in Class 530, subclass 300.

III. Claims 1-2, drawn to a polypeptide capable of binding a human IL-18; classified in Class 530, subclasses 350.

IV. Claims 1-38 and 44-46, drawn to antibodies or fragments thereof capable of binding a human IL-18 and a composition; classified in Class 530, subclasses 387.3, 388.22, and 389.1; and Class 424, subclasses 133.1 and 145.1

V. Claims 39-43, drawn to an isolated nucleic acid, a vector, a host cell, and a method of making an antibody by the host cell; classified in Class 536, subclass 23.1; and Class 435, subclasses 320.1, 325 and 69.1, respectively.

VI. Claims 47 and 49, drawn to a method for making an antibody by exposing an antibody repertoire to an antigen; classified in Class 435, subclass 7.1

VII. Claim 47-50, drawn to a method for making an antibody by immunizing an animal with the antigen comprising an epitope of human IL-18, classified in Class 424, subclass 184.1.

VIII. Claims 47, 49 and 51-52, drawn to a method for making an antibody wherein the antibody repertoire is a recombinant antibody library and the method comprises screening the library with an antigen comprising an epitope of human IL-18; classified in Class 435, subclass 69.1

IX. Claims 53, 55, 57, and 59, drawn to a method for inhibiting human IL-18 activity with a small molecule; classified in Class 424, subclass 600.

X. Claims 53, 55, 57, and 59, drawn to a method for inhibiting human IL-18 with a peptide; classified in Class 514, subclass 2.

XI. Claims 53, 55, 57, and 59, drawn to a method for inhibiting human IL-18 activity with a polypeptide; classified in Class 514, subclass 2.

XII. Claims 53-60, drawn to a method for inhibiting human IL-18 activity with an antibody; classified in Class 424, subclasses 133.1, 135.1 and 143.1.

Applicants hereby elect the Group IV invention (claims 1-38, and 44-46) drawn to antibodies or fragments thereof capable of binding a human IL-18 and a composition, for prosecution in this application, *with traverse* and request for rejoinder of Group IV with Groups II-III. Applicants further elect the species of antibody as Human and CDR specified by SEQ ID NOS.: 9, 10, 11, 12, 13, and 14.

It is Applicants' understanding that the species election is for searching purposes only and, upon a finding of allowability of the elected species, the remaining species also will be searched.

REQUEST FOR REJOINDER/RECONSIDERATION

Applicants respectfully request the modification of the Restriction Requirement to combine Groups II-IV for examination. First, Applicants assert that the subject matter of the various groups represent different embodiments for which a single patent should issue. Applicants have presented generic claim 1 which is directed to a compound capable of binding human IL-18 amino acid sequence. The *compound that binds to IL-18* can be a peptide, a polypeptide, an anti-IL-18 antibody, or antigen binding portion thereof. These compounds have the same effect, *i.e.*, they bind to IL-18 and modulate IL-18 activity. Thus, a peptide, a polypeptide, an antibody, or antigen binding portion thereof, operate by binding to an epitope on the IL-18 (*e.g.*, a compound is capable of binding a human IL-18 amino acid sequence, or portion thereof, where the amino acid comprises an N- or C-terminal portion of human IL-18 such as provided in SEQ ID NO: 67 or SEQ ID NO: 68, or, an isolated antibody, or an antigen-binding portion thereof, that binds an epitope of human IL-18 comprising amino acid provided in SEQ ID NO: 1 or SEQ ID NO: 33). Second, there must be a **serious burden** on the Examiner if restriction is not required. As the M.P.E.P. states:

> [i]f the search and examination of an entire application can be made without serious burden, the Examiner must examine it on the merits, even though it includes claims to distinct or independent inventions.

M.P.E.P. § 803.

The inventions of Groups II-IV have all been classified in Classes 530. As such, the searches with regard to these inventions would be co-extensive and would not involve a serious burden on the Examiner.

Furthermore, according to § 806.05 of the M.P.E.P., a "separate field of search" means, "it is necessary to search for one of the distinct subjects in places where no

pertinent art to the other subject exists" (*emphasis added*). Applicants respectfully request reconsideration of the requirement for restriction in the present application, as the examination of claims 1-38 and 44-46 together in the application would not place a serious burden on the Examiner, since the prior art search for Groups II-IV would be co-extensive (i.e., the field of search for these inventions will invariably contain much of the same relevant art).

Therefore, in the interest of savings of time and cost to Applicants and the Patent Office, Applicants request that the number of groups be reduced by combining Groups II-IV into a single group.

The Office Action, at page 4, indicates that Applicants, pursuant to 35 U.S.C. §121, are required to elect a specific type of antibody (e.g., monoclonal, polyclonal, or humanized).

Applicants wish to draw the Examiner's attention to the fact that the Applicants' invention is directed also to **human** anti-human IL-18 antibodies or antigen-binding portions thereof, wherein **the antigen-binding portion is human-derived.** Specifically exemplified in the application as filed are antibodies isolated from a scFv phage display cDNA library derived from human B cells. Human anti-human IL-18 single chain antibodies were isolated, characterized, and further modified (see Applicants' specification as filed; specifically page 30, line 20, to page 32, line 29, and Examples 1, 2 and 3, pages-36-49). Therefore, conforming to the disclosures made by the Applicants, Applicants hereby elect for type of antibody as "human" for examination. The Office Action further requires that the Applicants elect a specific CDR (i.e., a specific SEQ ID NOS).

The recognition properties of the antibody are carried by the variable regions (VH and VL). Each variable domain contains three hypervariable regions known as complementarity determining regions, or CDRs (e.g., CDR1, CDR2, and CDR3). The CDRs come together in the final tertiary structure to form an antigen-binding pocket. The sequence of exemplified single chain version of antibody 2E1 of the instant application, which binds to IL-18, is shown in Table 6 (page 29, lines 7-10). Each heavy and light chain of the antibody has three CDRs (CDR1, CDR2, and CDR3). These CDRs come together and bind to IL-18. Applicants believe that a *CDR election* refers to CDR interspersed from amino-terminus to carboxyl-terminus within the same antibody (*e.g.*,

anti-IL-18 antibody). Therefore, Applicants elect CDR specified by SEQ ID NOS: 9, 10, 11, 12, 13, and 14.

Claims 1-38 and 44-46 read on the elected antibody species and claims 25-28 read on the elected CDR SEQ ID NOS 9, 10, 11, 12, 13, and 14.

Applicants understand that the election is made solely for the purpose of examination, and that they will be entitled to consideration of claims to additional species upon allowance of a generic claim. Applicants also reserve the right to traverse the restriction between the non-elected groups and species in this or a separate application.

If a telephone conversation with Applicants' attorney would help expedite the prosecution of the above-identified application, the Examiner is urged to call the undersigned attorney at (617) 227-7400.

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Dated: March 18, 2002